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Dear Linus

I have just had my first opportunity of really studying your "antibody" paper in the August J. Exp. Med. and am writing you because of some rather disquieting reservations that seem indicated.

Let us take, for example, the "most promising" alkali-denaturation experiment with methyl blue: Would a control, without dye, show appreciable loss of nitrogen as ammonia? Is anything known about the sensitivity of γ -globulin under these conditions?

All in all, this experiment shows only that a sample of globulin, in longer contact with dye and alkali, binds more dye than one in shorter contact. In view of our ideas on the mechanism of specific precipitation and antigen-excess solubility, which are only special cases of precipitation and solution in general, hapten effects are to be expected whether or not antibody has been produced. Again, I think, Deen's experiments with Isamine Blue and normal sera, showing a complete parallel with immune precipitation, are very pertinent as an analogy.

I was also greatly disturbed to find that the arsenic-azo material fails to precipitate south of pH 6.5. While it is quite remarkable that your product shows as great similarity to antibody as it does, true antibodies react with homologous antigen independently of pH between roughly 5 and 9—a really enormous range of H ion concentration. Is it not, therefore, stretching a point to call your altered globulin "antibody"? Again there is a very disturbing analogy: the precipitation of non-antibody (Pn type-specific) globulin in antipneumococcus horse sera (J. Immunol., 1941, 40, 1) by nucleic acid, which is both pH- and salt-sensitive. Again, I do not think solubility in excess hapten ^{in these} arsenic dye experiments necessarily indicates the involvement of antibody.

The pneumococcus III experiments do not seem to decide any of these questions, either.

I do hope you will not mind these reservations, because you know I would like to see a real, airtight ^{confirmation} of what I consider a brilliant deduction, and think you will want to furnish such evidence in your next publication.

With all good wishes,

Sincerely

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